

Klinefelter's Syndrome and sexual offending- a literature review.

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Abstract

Background: Klinefelter's Syndrome is a sex chromosome abnormality affecting approximately 1 in 1000 males. There have been suggestions that it is associated with a higher than average prevalence of sexual offending but to what extent does research evidence support this assertion?

Aims: To conduct a systematic review of published research to establish the prevalence of sexual offending in males with Klinefelter's Syndrome.

Method: The databases MEDLINE, PsycINFO and EMBASE were searched from inception until 31st December 2016 using a range of terms for Klinefelter's syndrome and for sexual offending. All selected papers were examined for quality using the STROBE (Strengthening of Observational Studies in Epidemiology) checklist.

Results: We identified 53 relevant papers of which ten met our inclusion criteria. All but one were prevalence studies conducted in a prison or hospital setting. The one, Danish, register based cohort study did suggest an increased risk of sex offending among Klinefelter men, probably established before the diagnosis was made and, therefore, any hormone replacement instituted.

Conclusion: There is insufficient evidence to date to support concerns about exceptional risk of sex offending among men with Klinefelter's syndrome. Rather, it is arguable that there is a research gap in understanding how the experience of and treatment for their condition may affect them.

Introduction

Klinefelter's Syndrome is a genetic disorder, which affects the sex chromosomes. It occurs in 1/500 to 1/1000 male births, invariably conferring at least one extra female (X) chromosome. There are several genotypes, which include 47 XXY (almost 90% of cases), 48 XXXY and 49 XXXXY, or various mosaics, and the abnormal presence of Barr Bodies, which are inactive X chromosomes in female somatic cells, absent in typical males (Pacenza et al., 2012). Phenotypically, men and boys with Klinefelter's tend to be taller than average but with a female body shape. They have enlarged breasts, often fail to develop secondary sexual characteristics, such as pubic hair, and have small testicles; they are usually (but not always) infertile. They tend to experience low libido and impotence. These bodily characteristics are thought to be a consequence of low testosterone levels, also associated with increased risk of osteoporosis – a form of fragile bones - in adult males (Smyth and Bremner, 1998). Management has, therefore, been focused mainly on these features. Most literature suggests that treatment with testosterone may reduce the risk of osteoporosis and improve sexual function. Although there is some dissent with respect to osteoporosis (Ferlin et al 2010, Wong et al 1993) and sexual function (Hwang & Lin 2008), early diagnosis and treatment with testosterone in puberty are recommended (Bojesen and Gravholt 2007).

While it may be appropriate to begin androgen replacement therapy, treatments are rarely without side effects and it has been suggested that, despite many men with Klinefelter's syndrome experiencing some form of sexual dysfunction, such replacement may increase their risk of sexual offending (Wakeling, 1972, Mosier et al., 1960, Harrison et al., 2001). Further, there is currently no guidance for the management of patients in these circumstances.

Aims

Our aim was to undertake a systematic review of published literature examining the relationship between sexual offending and Klinefelter's Syndrome. Our research question was: Is there research evidence of a higher prevalence of sex offending among men with Klinefelter's syndrome than among XY men?

Method

Searches of the databases MEDLINE, PsycINFO and EMBASE were conducted using the following algorithm: [(‘Klinefelter’s Syndrome’) OR (‘Klinefelter’) OR (‘Klinefelter’s’) OR (‘XXY’) or (‘XXYY’) or (‘XXXY’)] AND [(‘sex offending’) OR (‘sexual offending’) OR (‘sexual deviance’) OR (‘sexual assault’) OR (‘sexual behaviour’) OR (‘Offence’) OR (‘Offend\$’)]. In addition searches of the Cochrane library, the York Research Database and Google were undertaken. Time scale was from the earliest database record until 31st December 2016. Studies involving patients of any age, with any of the karyotypes of Klinefelter’s Syndrome, and all categories of sexual offending were included. Studies in all languages were considered. No study type was excluded at this stage. Citations in reference list of relevant papers were hand searched in order to identify any additional references of interest. Study quality of all included studies was compared using the STROBE statement checklist, a 22 item checklist used to assess the quality of the studies (Von Elm et al 2008).

Titles and abstracts were read by the first author and were checked by the second. Papers were excluded if they did not include sexual offending or made no specific reference to Klinefelter’s Syndrome, or they were single case reports. As many of the papers were several decades old, some of the legal and clinical definitions for sexual offending were out of date; therefore papers that were only about prevalence of homosexuality, transsexual or transgender behaviour were excluded.

Results

Fifty-three papers were identified through electronic searches. After reading the abstracts, 47 papers were considered to be potentially relevant but, after reading the full text, only eight met the inclusion criteria. Three papers had to be excluded because they were no longer available; the British Library attempted to source copies without success. Hand searching identified a further six papers of potential relevance, of which two met our inclusion criteria.

This review, therefore, draws on ten articles. Nine were from prison or hospital communities, whilst one (Stochholm) was a register based cohort study. The table provides a summary of the papers. Studies reporting from prisons or forensic mental health services generally compared the offending behaviour of

Klinefelter men with XYY men, although a direct comparison was made with the general prison population in some instances. There was, however, no consistency of comparison group due to variation in sampling methodologies used. The one cohort study suggested a nearly threefold increase in risk of sexual offending among Klinefelter males in comparison to age and calendar matched samples in the general population.

Discussion

Thus, the suggestion of an increased risk of sex offending is supported, but by only one register based cohort study in one European country. This study was conducted in Denmark, from where five of the 'treated sample' studies had emerged. It is not clear whether the increased risk was associated with treatment with testosterone or if so, whether the treatment was adequately monitored. Although, Stockholm et al (2012) did try to consider the impact of participants receiving treatment with testosterone on their results they could only do this indirectly by looking at the rates of offending before and after diagnosis. They found that the prevalence of sexual offending was higher before diagnosis. This is of particular relevance as there is evidence to suggest that there may be a relationship between exogenous testosterone and sexual offending (Raboch et al 1987). There is no evidence from the study included here that treatment with testosterone increased the risk of sexual offending in Klinefelter men.

All other reported studies have been conducted with highly selected populations. Nielsen et al (1969a) and Baker et al (1970) both selected participants on the basis of height and then completed cytogenetic screening for the participants; Wakeling (1971) selected on the basis of other abnormalities in appearance. It has subsequently been estimated that only 25% of Klinefelter cases are diagnosed (Stochholm et al 2012), so in these highly selected samples, the chromosomal variation and/or treatment may have been only indirectly responsible for any offending behaviours. Theilgaard (1984), again in Denmark, having identified XYY and XXY men in a 1944-47 birth cohort, found men in both the abnormal chromosome groups had been arrested but not convicted more frequently than those in the general population, but had also reported poorer childhood experiences on a number of standardized measures, though they included all offending and not sexual offending alone.

Although (Bojesen and Gravholt 2007) recommended early treatment with testosterone, case reports described by Raboch et al (1987) and Sourial and Fenton (1988) illustrate that sexual dysfunction does not always occur in this group. Yoshida et al (1997) found that 90% of Klinefelter males included in their study had a normal libido and 97.5% were able to sustain an erection during intercourse. They concluded that there was no difference between the frequencies of sexual function disturbances in these groups. Further, there are mixed views on the effectiveness of hormonal treatment. Some have suggested that use of androgen replacement is not particularly effective for managing the physical health complications of androgen deficiency (Ferlin et al 2010), but others have concluded that androgen replacement therapy improves the physical health of Klinefelter men (Bojesen and Gravholt 2007) in addition to their mental health (Zarrouf et al 2009) and sexual function (Vignozzi et al 2010).

An absence of consensus on the value and risks of treatment for Klinefelter's syndrome together with single country data on the association between the condition and sex offending drawn from a population based sample, may pose an ethical dilemma for the treatment of some men with Klinefelter's syndrome. Whilst it has been reported that there is no temporal relationship between testosterone level and the intensity of sexual desire (Hwang and Lin 2008), there is evidence to support the use of testosterone to improve libido and sexual function in those patients who experience sexual dysfunction (Vignozzi et al 2010). Treating men with testosterone after they have committed a sexual offence may be at odds with Guidelines for the Biological Treatment of Paraphilias (Thibaut et al., 2010), in which it is suggested that successful treatment of sex offenders is achieved through maintaining a hypogonadal state. There is, however, no evidence from our review that treatment with testosterone increases the risk of sexual offending in Klinefelter men.

Conclusion

Our literature review merely confirmed the scant evidence on which claims about an increased risk of sex offending by men with Klinefelter's syndrome are based. In particular, there is an absence of sound longitudinal work mapping the relationship over time between the advocated testosterone replacement therapy and any unwanted sexual behaviours. In remedying this in the future, it will be important to explore the impact of this disorder on an individual's social and psychosexual functioning as such experiences are of significance when considering offending behavior.

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Table 1 Summary of papers

Date	Author	Participants	Setting	Method	Results
1960	Mosier et al	10 KS 407 LD controls ('mental defectives') Admitted between 1948 and 1952	State hospital, Los Angeles, USA	Comparison of prevalence of sexual offending in two groups. Both groups were divided into IQ ranges.	Incidence of sexual offending: 70% (n=7) KS group, 13.5% (n=55) control group. Statistically significant higher incidence of sex offending in KS remained when matching for IQ.
1969 (a)	Nielsen et al	5 KS 3 XYY 2 46, XY mosaics	Horsens State Prison, Denmark	Prevalence and incidence study of Klinefelter's and XYY. Prevalence study--blood samples for 135 out of 217 men (chosen from the 'tallest and most immature'). Incidence study--blood samples from 97 out of 108 men (inclusion criteria not described). Criminal offences compared between groups.	History of sexual offending: 30% (n=3) of KS, 20% (n=2) of XYY. 16% (n= 39) in general prison sample.
1969 (b)	Nielsen et al	34 KS 16 Hypogonadal males	Hypogonadism Study Section at the outpatients clinic, Copenhagen University Hospital	Comparison of intelligence, personality, mental health and criminality in KS and hypogonadal males.	History of sexual offending: 5.8% (n=2) KS patients, 1 hypogonadal patient accused of sexual offence against a child, no charges brought.
1970	Baker et al	8 KS 7 XYY Identified from sample of 876	Prison, psychiatric & learning disability populations, USA.	Cytogenetic screening. Comparison of prevalence of sexual offending between groups.	Prevalence of sexual offending: 87% (n=7) KS patients, 71% (n=5) XYY patients. Sexual offending in controls not documented.
1970	Nielsen	61 KS, 12 XYY of whom 28 KS, 11 XYY history of 'major criminality with violation of the penal code.'	Psychiatric hospitals, neurological, medical & surgical wards and 'institutions for criminal psychopaths', Denmark	Comparison of offending in two groups (offending only registered if charged)	Frequency of sexual offending: 43% (n= 12) of 28 KS, 45% (n= 5) of 11 XYY patients. Results compared with sentenced males, Denmark, 1966 (n = 6598), and 'mentally retarded' males. Frequency of sexual offending 7% and 27% respectively.
1971	Nielsen	1 KS 4 XYY 206 controls	198 men from a forensic psychiatric clinic and psychiatric hospital, Denmark.	Comparing prevalence and incidence of chromosome abnormalities in a forensic psychiatric population.	One KS participant and none of the XYY participants had committed a sexual offence. 34 (17%) of controls had committed a sexual offence.
1972	Nielsen et al	2 KS	Youth prison,	Chromosome analysis	One prisoner with KS and

	al	3 XYY out of 146 controls admitted any time Feb 1969- Oct 1970	Møgelkær, Denmark	study. Comparison of sexual offending between groups.	none of the XXY males had committed a sexual offence. Sexual offending amongst controls not reported.
1972	Wakeling	11 KS 9 Hypogonadal controls Over 15 years (dates not specified).	Bethlem Hospital, UK	Review of case records to assess impact of Klinefelter's Syndrome on psychopathology.	History of sexual offending: 18% (n=2) KS patients, none of the controls
1981	Schröder et al	11 KS 9 XYY 1019 offenders undergoing mental examination	3 psychiatric hospitals, Finland	Sex chromatin screening. Comparison of offending in two groups.	History of sexual offending: 27% (n=3) KS 22% (n=2) XYY 18% (n=184) prisoners in control group.
2012	Stochholm et al	934 KS were compared with 88,979 general population controls. Study population was identified from Danish Cytogenetic Register.	Denmark	Register based cohort study comparing the incidence of convictions among men with KS and XYY with age matched controls in the general population.	Incidence of convictions for sexual abuse, including rape: 26 KS, 592 controls. Hazards ratio in KS (HR) 4.04 (95% CI 2.71 to 5.95). After adjustment for socioeconomic variables HR 2.72 (95% CI 1.60 to 4.69)

KS- Klinefelter's Syndrome

CI – Confidence interval